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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,545	12/17/2003	Masahiro Kawaguchi	03500.017338	6817

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,545	KAWAGUCHI ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6,7,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 6, 7, 28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1, 3-5, and 8-27 have been canceled as filed on 9/10/07.

Claims 2, 6, 7, 28 and 29 are currently pending.

Claim 27 has been withdrawn.

Claims 2, 6, 7, 28 and 29 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group II (Claims 2-7) in the reply entered on 11/14/2005 was previously acknowledged.

3. Applicants also elected the following species as previously acknowledged:

A.) fluorescent markers;

B.) two kinds of external standard probes;

C.) one kind of internal standard probes;

D.) single-stranded DNA;

E.) 20 residues each of internal and external probes;

F.) two sets of primers that will produce 500 bp and 200 bp products;

G.) a "microorganism'" is selected as the most specific species explicitly recited in the specification;

H.) one nucleic acid;

I.) two.

Priority

4. This application appears to be a CONTINUATION of PCT/JP03/07918 filed on 6/23/03.

Receipt is acknowledged of the following papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file:

A.) An application filed in JAPAN (2002-191390) on 6/28/2002.

B.) An application filed in JAPAN (2002-183249) on 6/24/2002.

Information Disclosure Statement

5. The IDS filed on 8/27/07 has been considered. See the attached PTO 1449 form.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Dudley et al

7. Claims 2, 6, 7, 28 and 29 are rejected under 35 U.S.C. **102(b)** as being anticipated by Dudley et al (PNAS. Vol. 99: 7554-7559. May 28, 2002 (cited previously) and the accompanying "Supplementary Material" downloaded from

//arep.med.Harvard.edu/masliner/supplement.htm). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

The instant claims briefly recite "a DNA micro-array for detecting nucleic acid molecules having target base sequences in a samples, said array comprising:

a substrate; and

nucleic acid probes including base sequences complementary to the target base sequences, the nucleic acid probes being immobilized on the substrate,

wherein the array contains at least two probes for internal standard nucleic acids, said at least two probes having different sequences from each other and having sequences complementary to the internal standard nucleic acids,

wherein said at least two probes are available for quantitative evaluation of PCR of said nucleic acid molecules having the target base sequences, and

wherein said at least two probes include at least two probes corresponding to PCR products with different chain lengths derived from the internal standard nucleic acids."

The specification of the instant application discloses the internal standard probe as "a probe for detecting an internal standard nucleic acid to be used to assist quantitative determination of a target nucleic acid," and the internal standard nucleic acid as "a nucleic acid of a known base sequence" (page 12 of the specification). The external standard nucleic is also disclosed as "a nucleic acid having a known base sequence to be added to a sample..." and "has no base sequence homology to the base sequence of the target nucleic acid." Therefore, the internal and the external standards and probes could be any nucleic acid sequences that are known, and are not complementary to the target sequences.

The recitation "quantative evaluationof PCR" is construed as intended use for the claimed product of a DNA microarray.

Dudley et al, throughout the publication, teach measuring absolute expression with microarrays with a calibrated reference sample, and generating ratios between sample intensities

and intensities of the oligo reference measure sample RNA levels (See Abstract of the reference). The reference teaches microarrays comprising probes generated from yeast ORF PCR product set, and an oligo reference sample with certain nucleic acid sequence (See page 7554, right column, 4th paragraph of the reference). The yeast ORF PCR product set contains over 6,000 yeast ORF (see the "Supplementary Material" (p. 9 of Supp.) described on p. 7555, left column, last paragraph of the reference), which could contain the "target nucleic acid" (could be any yeast gene of interest from the >6,000 ORF PCR products). The oligo reference sample could be either the "internal" or "external" probes for the internal or external standards since the oligo sequence is known and contained on the microarray. In addition, any other probes for the >6,000 genes that is not the considered to be the gene of interest (the target gene) and is not complementary to the target gene sequence could be considered as either the internal or the external probes. For example, the RPL29, or the PHO88 genes listed in Figure 3 on Page 7557. The probes for these genes on the microarray would hybridize to genes with different PCR products (different lengths). The reference further teaches that the microarray are generated either by printing PCR generated cDNA or commercially available oligo sets (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which would refer to synthetic nucleic acids immobilized on the substrate, and different sequences placed at different positions of **clm 2** because each of the probes is printed at a different spot (see the Supplementary Figure 4). In addition, the reference teaches the oligo reference sample is 20 bases long (page 7554, right column, 4th paragraph of the reference), which would refer to nucleic acid has a chain length of 15 to 75 bases, as recited in **clm 7**. The reference further teaches the Yeast Genome Oligo Set were printed at a concentration of 10 pmols/ml in 150 mM

potassium phosphate (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which reads on probes with the same concentration of **clm 29**. The reference also teaches teaches that the microarray are generated either by printing PCR generated cDNA or commercially available oligo sets (See Supplemental Web Site as described on p. 7555, left column, last paragraph of the reference), which reads on the synthetic nucleic acids immobilized on the substrate as recited in **clm 6**. The reference also teaches resuspending the various PCR products in 150 mM potassium phosphate (Supplemental Material, p. 9), which reads on "spots having different concentrations" of **clm 28**.

The probes (or "internal probes") taught by the reference also reads on the inherent property of "corresponding to PCR products with different chain lengths" as recited in **clm 2**, because the probes can hybridize to target molecules with different chain lengths. For example, a probe on the array with 20 nucleotides complement to a target molecule with 30 nucleotide length (comprising the 20 nucleotide complement to the probe) would also be complement to a target molecule with 40 nucleotide length (comprising the same 20 nucleotide complement to the probe). In other words, the recitation "corresponding to PCR products with different chain lengths" does not offer any additional structural limitation to the claimed probes.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the reference does not teach all element of the claimed invention. (Reply, p. 4, para 3).

Applicants are respectively directed to the above rejection for detailed discussion on how the cited reference teach each and every element of the instant claimed invention.

Applicants also assert that the reference does not teach the following "features"of the claimed invention. (Reply, p.4 para 4).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "select a PCR product of an internal standard nucleic acid that has the same chain length as the PCR product of the nucleic acid molecule having the target base sequence") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Delenstarr et al

9. Claims 2, 6, 7, 28 and 29 are rejected under 35 U.S.C. **102(b)** as being anticipated by Delenstarr et al (US PGPUB 2002/0051973 A1; May 2, 2002; cited previously). The previous rejection is maintained for the reasons of record as set forth in the previous Office action.

Delenstarr et al, throughout the publication, teach a set of features comprising oligophophodiester probes (reads on microarrays of **clm 2**; Claim 1 of the reference). The reference teaches hybridization features comprising hybridization probes (bound to a surface;

Claim 2 of the reference) that selectively hybridize to a detectably labeled target nucleotide sequence (reads on the probes for the target nucleic acid of **clm 2**; Claim 1 of the reference). The reference also teaches background features comprising background probes (as listed in Claim 4 of the reference) that do not selectively hybridize to said nucleotide sequence (read on the internal and/or external probes of **clm 2**; Claims 2 and 4 of the reference). In addition, the reference teaches the features (or array) comprising target probes, test-background probes (read on either internal or external probes of **clm 2**), and standard-background probes (read on either internal or external probes of **clm 2**); (See Claim 30 of the reference). The reference also teaches the probes could be 25 bases long (such as SEQ ID NO 5 as recited in Claim 5, for example), which reads on the length recited in **clm 7**. Furthermore, the reference recites various different probes with different sequences (such as the one directed in Claim 5 of the reference), which have the functions of hybridizing to PCR products with different chain lengths. The reference further teaches that the probes can be synthesized (See paragraph [0104] of the reference), which reads on limitation of **clm 6**. The reference also teaches printing the probes on different spots (e.g. Figure 3), which reads on the different positions of **clm 2**. The reference also teaches the concentration of different probes on the microarray (e.g. Example 6, p. 15+; especially p.11), which reads on the spots having the same or different concentrations of **clms 28 and 29**.

The probes (or "internal probes") taught by the reference also reads on the inherent property of "corresponding to PCR products with different chain lengths" as recited in **clm 2**, because the probes can hybridize to target molecules with different chain lengths. For example, a probe on the array with 20 nucleotides complement to a target molecule with 30 nucleotide length (comprising the 20 nucleotide complement to the probe) would also be complement to a

target molecule with 40 nucleotide length (comprising the same 20 nucleotide complement to the probe). In other words, the recitation "corresponding to PCR products with different chain lengths" does not offer any additional structural limitation to the claimed probes.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the Dudley reference. Thus, applicants are respectively directed to the discussion under the Dudley reference for answer to arguments

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
10/12/07

/Jon D. Epperson/
Primary Examiner, AU 1639